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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,802	09/17/2001	Roland Kreutzer	33796	8835

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PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER

WHITEMAN, BRIAN A

ART UNIT PAPER NUMBER

1635

DATE MAILED: 04/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/889,802

Applicant(s)

KREUTZER ET AL.

Examiner

Brian Whiteman

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 221-247 is/are pending in the application.
- 4a) Of the above claim(s) 226-231 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 221-225, 232-239, 241-243 and 245 is/are rejected.
- 7) ☐ Claim(s) 240, 244, 246 and 247 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 September 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11, 15. 6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 221-225 and 232-247 are pending examination.

The addition of claims 239-247 in paper no. 19 is acknowledged and considered.

The amendment to the title, the addition of claims 221-238, and the cancellation of claims 126-220 in paper no. 16 is acknowledged.

The deletion of claims 1-125 in paper no. 14 is acknowledged.

The amendment to the specification in paper no. 10 filed on 9/17/01 has not been entered because it is missing a marked-up copy of the amendment. See 37 CFR 1.121.

The international search report has been considered.

Election/Restrictions

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 221-225 and 232-238, drawn to an oligoribonucleotide having a double stranded structure (dsRNA) comprising two separate RNA strands wherein one of the dsRNA has a region which is complementary to an RNA transcript of at least a part of a target gene, wherein the region is not more than 49 nucleotides in length, and wherein the target gene is a mammalian gene and a mammalian cell comprising said oligoribonucleotide, wherein the oligoribonucleotide was transfected into the cell.

Art Unit: 1635

Group II, claim(s) 226-231, drawn to a method of inhibiting the expression of a target gene in a mammalian cell, the method comprising: (a) introducing into a cell an oligoribonucleotide having a dsRNA comprising two separate RNA strands wherein one of the dsRNA has a region which is complementary to an RNA transcript of at least a part of a target gene, wherein the region is not more than 49 nucleotides in length; and (b) maintaining the cell produced in step (a) for a time sufficient to obtain degradation of an RNA transcript of the target gene, thereby inhibiting expression of the target gene in the cell.

The inventions listed as Groups I-II do not relate to a single inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they lack the same or corresponding technical feature for the following reasons:

The technical feature linking groups I-II appears to be that they all relate to an oligoribonucleotide having a double stranded structure (dsRNA) comprising two separate RNA strands wherein one of the dsRNA has a region which is complementary to an RNA transcript of at least a part of a target gene, wherein the region is not more than 49 nucleotides in length, and wherein the target gene is a mammalian gene.

However, Shimkets et al. (US Patent No. 6,486,299, EFD 9/28/1999) teaches a human GENE SET anti-sense nucleic acids that are at least six nucleotides (more preferably 6-50 nucleotides) complementarily to a coding or non-coding region of a human gene and may be double stranded (column 17, lines 19-60).

Therefore, the technical feature linking the inventions of groups I-II does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art.

The special technical feature of Group I is considered to be an oligoribonucleotide.

The special technical feature of Group II is considered to be a method of inhibiting the expression of a target gene in a mammalian cell, the method comprising using an oligoribonucleotide.

Accordingly, Groups I-II are not so linked by the same or a corresponding technical feature as to form a single inventive concept.

During a telephone conversation with Kathleen Williams on 3/3/03, a provisional election was made with traverse to prosecute the invention of Group I, claims 221-225 and 232-238.

Affirmation of this election must be made by applicant in replying to this Office action. Claims 226-231 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being

drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made **with** traverse.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications filed in German on 1/30/99 and 11/24/99. It is noted, however, that applicant has not filed a certified copy of the 19903713.2 and 19956568.6 applications as required by 35 U.S.C. 119(b).

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

The disclosure is objected to because of the following informalities: On page 9, a description of Figure 4B-4E is missing.

The disclosure is objected to because of the following informalities: the specification may not to refer to claims. See page 1, line 5 and page 2, lines 31-33. Suggest incorporating the content of the claims into the specification.

In addition, the disclosure is objected to because of the following informalities: The heading of each section is missing.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Art Unit: 1635

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
- (e) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (f) BRIEF SUMMARY OF THE INVENTION.
- (g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (h) DETAILED DESCRIPTION OF THE INVENTION.
- (i) CLAIM OR CLAIMS (commencing on a separate sheet).
- (j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Appropriate correction is required.

Claim Objections

Claim 243 is objected to because of the following informalities: reciting an improper grammatical phrase "an oligoribonucleotide according to claim 221." Suggest replacing the

Art Unit: 1635

phrase with -- the oligoribonucleotide according to claim 221--. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 241 and 242 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 241 and 242 are indefinite because claim 241 depends on itself. Claim 242 is dependent from claim 241 and the metes and bounds of the claim are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

Art Unit: 1635

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 221, 222, 224, and 243 are rejected under 35 U.S.C. 102(e) as being by Shimkets et al. (US 6,486,299, EFD 9/28/98). Shimkets teaches a human GENE SET anti-sense nucleic acids that are at least six nucleotides (more preferably 6-50 nucleotides) complementarily to a coding or non-coding region of a human gene and may be double stranded (column 17, lines 19-60).

Claims 221, 222, 223, 232, 233, 234, 235, 236, and 243 are rejected under 35 U.S.C. 102(e) as being by Fire et al. (US 6,506,559, EFD 12/23/97). Fire teaches an oligoribonucleotide having a double-stranded structure comprising two separate RNA strands, wherein one strand of the dsRNA has a region, which is complementary to an RNA transcript of a portion of a target gene from a mammalian gene, wherein, the region is at least 25 bases (columns 8 and 26-28). The RNA may be synthesized in vivo or in vitro (column 8, line 62 – column 9, line 25). Fire further teaches mammalian cells containing the oligoribonucleotide (column 8, line 52 – column 9, lines 48).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 221, 232, 239, and 245 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (US 6,506,559, EFD 12/23/97) taken with Pasloske et al. (US Patent 5,939,262, EFD 6/24/97). Fire teaches an oligoribonucleotide having a double-stranded structure comprising two separate RNA strands, wherein one strand of the dsRNA has a region, which is complementary to an RNA transcript of a portion of a target gene from a mammalian gene, wherein, the region is at least 25 bases (columns 8 and 26-28). Fire further teaches mammalian cells containing the oligoribonucleotide (column 8, line 52–column 9, line 48). However, Fire does not specifically teach modifying the double stranded RNA so as to be resistant to RNA degradation.

Art Unit: 1635

However, at the time the invention was made, Pasloske teaches modifying double stranded RNA so as to be resistant to ribonuclease (column 5, lines 1-24 and column 7, lines 1-20).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to modify the double stranded RNA so as to be resistant to RNA degradation. One of ordinary skill in the art would have been motivated to modify the double stranded RNA to be resistant to RNA degradation to improve the stability of the double stranded RNA in a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 221, 224, 225, 232, 237, and 238 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (US 6,506,559, EFD 12/23/97) taken with Jaschke et al., (Nucleosides & Nucleotides, Vol. 15, pages 1519-1529, 1996). Fire teaches an oligoribonucleotide having a double-stranded structure comprising two separate RNA strands, wherein one strand of the dsRNA has a region, which is complementary to an RNA transcript of a portion of a target gene from a mammalian gene, wherein, the region is at least 25 bases (columns 8 and 26-28). Fire further teaches mammalian cells containing the oligoribonucleotide (column 8, line 52–column 9, line 48). However, Fire does not specifically teach using a polyethylene glycol linker (PEG) to link the two RNA strands.

However, at the time the invention was made, Jaschke teaches using PEG to link RNA strands to make them more stable towards exonucleolytic degradation (pages 1519-1521 and 1522-1527).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to link the double stranded RNA using a PEG linker. One of ordinary skill in the art would have been motivated to link the double stranded RNA using a PEG linker to make them more stable towards exonucleolytic degradation.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Conclusion

Claims 240, 244, 246, and 247 are free of the prior art.

Claims 240, 244, 246, and 247 are objected to as being dependent upon a rejected base claim (claims 232 and 221), but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

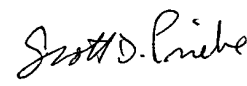
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Art Unit: 1635

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635


SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER